

# Department of Ophthalmology

## Chair of Ophthalmology

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### Director

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### Research focus

- Biomorphometry of the optic nerve
- Functional aspects of retinal neurodegeneration
- Retinal physiology
- Clinic-pathological concepts in diagnosis and management of ocular diseases
- Corneal stem cells
- Pseudoexfoliation syndrome/glaucoma
- Improvements in corneal transplantation
- Circulation of the eye and the visual pathway, computer-aided-diagnosis, and virtual education

### Structure of the Department

Professorships: 9

Personnel: 172

- Doctors (of Medicine): 43
- Scientists: 13 (thereof funded externally: 7)
- Graduate students: 57

### Clinical focus areas

- Surgery of the frontal eye
- Cornea surgery
- Reconstructive surgery of the frontal eye
- Glaucoma seamless transconjunctival retinal vitreal surgery (23-gauge-vitreotomy)
- Minimal invasive glaucoma surgery employing implants
- Refractive surgery with the femtosecond laser
- Cataract surgery with innovative intraocular lenses
- Intraocular injections of compounds to treat age related macular degeneration (AMD)
- Special consultation
- Departments of optometry, fluorescence angiography, and laser
- Outpatients' department
- Cornea bank
- Laboratories

### Research

The Department of Ophthalmology belongs to the leading centers in the areas of lamellar corneal transplantation including structural biology of the cornea as well as diagnostics and pathophysiology of glaucomas at a national and international level. An interdisciplinary team of clinician and basic scientists conducts patient-oriented experimental and clinical research into corneal disorders, neurodegenerative diseases, such as glaucoma, and ocular tumors. The broad spectrum of methodologies applied includes molecular and cell biologic experiments, histology and electron microscopy, electrophysiology and visual psychophysics, and state-of-the-art imaging modalities, such as OCT angiography and magnetic resonance imaging. New medical devices for treatment of ocular diseases are being tested as part of multicenter studies. The major goal of the research efforts is to elucidate the pathophysiological causes underlying degenerative and vascular diseases of the eye and visual pathway on a molecular, cellular, and systemic level, to advance the microsurgical techniques, to secure the quality of treatments, and to promote the development of novel therapeutic concepts and treatment strategies.

#### Biomorphometry of the optic nerve

PI: Prof. Dr. C. Mardin, PD Dr. R. Lämmer, Dr.-Ing. R. Tornow

Main focus of the research is the development and application of imaging methods for early detection of glaucoma and to quantify progression. Especially the possibilities of the spectral domain OCT (optical coherence tomography) to measure retinal layers will be optimized. The developed imaging methods are complemented by functional tests. The findings are also applied to other diseases, like diabetic retinopathy and AMD.

#### Functional aspects of retinal neurodegeneration

PI: Prof. Dr. J. Kremers, Dr.-Ing. F. Horn, Dr. C. Huchzermeyer

In this research project, new electrophysiological and psychophysical techniques are developed to study the functional aspects of retinal degeneration, especially of glaucoma. Electrophysiological tests are objective and allow a direct assessment of retinal pathophysiology. Psychophysical tests can be very sensitive and give an impression about perceptual changes in patients. Novel methods are developed to accu-

rately study the responses that are elicited by single photoreceptor types or by different retinal pathways. Innovative developments in the multifocal stimulation technique and in perimetry are implemented to allow an early diagnosis of retinal degeneration.

#### Retinal physiology

PI: Prof. Dr. J. Kremers

The goal of this working group is to study the function of the normal and diseased retina. To reach that goal, we record electrophysiological responses of the retina of rodent models of human diseases. In addition, we perform electrophysiological and psychophysical experiments with normal human test persons and patients to identify different signal pathways in the retina and the changes caused by a disease. The results of the animal and human experiments are related with each other so that the pathophysiological processes can be better understood.

#### Clinicopathologic concepts in diagnosis and management of ocular diseases

PI: Prof. Dr. L. Holbach, Prof. Dr. F.E. Kruse, Prof. Dr. G. Gusek-Schneider, Prof. Dr. A. Bergua

1. Diagnosis and management of orbital diseases – a multidisciplinary approach
2. Surgical management of periocular malignant tumors using frozen section control and plastic reconstruction – indications, methods, and results
3. Diagnosis and surgical management of epibulbar lesions

The purpose of this study is to establish correlations between morphologic, biomicroscopic, histologic, and molecular genetic criteria and the long-term results of surgical excision and plastic reconstruction.

#### Corneal stem cells

PI: Prof. Dr. U. Schlötzer-Schrehardt, Prof. Dr. F.E. Kruse

Transplantation of cultivated limbal epithelial progenitor cell grafts has been used to restore epithelial defects of the human cornea in patients with limbal stem cell deficiency. This research project explores the molecular characteristics of corneal stem and progenitor cells together with their specific niche microenvironment and their utilization for improved stem cell based therapies on tunable biosynthetic matrices. The applicability of alternative autologous stem cell sources for corneal epithelial tissue engineering strategies is also investigated.

### **Pseudoexfoliation syndrome/glaucoma**

PI: Prof. Dr. U. Schlötzer-Schrehardt

Pseudoexfoliation (PEX) syndrome is worldwide a leading cause of chronic open-angle glaucoma. The focus of this research project is the molecular analysis of the underlying, genetically determined, fibrotic process through functional characterization of the PEX-associated coding and non-coding risk variants in the LOXL1 (lysyl oxidase-like 1) gene as well as the interaction of LOXL1 with profibrotic mediators, such as TGF $\beta$ 1, oxidative stress, and mechanical stress.

### **Development of new methods for lamellar corneal transplantation**

PI: Prof. Dr. F.E. Kruse, Prof. Dr. T. Fuchsluger, Dr. Tourtas, Dr. J. Menzel-Severing

The Department of Ophthalmology has an internationally leading position in the performance and advancement of new minimally invasive techniques of lamellar corneal transplantation, such as DMEK (Descemet Membrane Endothelial Keratoplasty), using grafts consisting of a single cell layer to replace the diseased corneal endothelium. The clinical research group focuses on the further development of pre-, intra-, and postoperative strategies and the analysis of clinical outcomes to continuously improve quality and reproducibility of the new surgical techniques.

### **Circulation of the eye and the visual pathway, computer-aided diagnosis, and virtual education**

PI: Prof. Dr. G. Michelson

#### **1. Ocular circulation of the eye and the visual pathway**

The tissues and vessels of the eye reflect systemic diseases and are a perfect system for the visualization of physiologic processes of the body. Immunological processes, diabetes, and arterial hypertension can be evaluated quantitatively in the eye.

#### **2. Computer-aided-diagnosis and virtual education**

Ophthalmology needs new methods for medical information processing to optimize diagnosis and therapy. Automated analysis of ophthalmic images combined with automated classification leads to a fast and bias-free evaluation, which is an important prerequisite for screening.

3. Diffusion measurement of the visual pathway based on magnetic resonance images neurodegenerative eye diseases often involve the entire visual system. In some cases, they are induced by a cerebral macro- and microangiopathy with

subsequent ischemic changes and degeneration of the visual pathway. The new non-invasive technique based on magnetic-resonance imaging provides information about the integrity and orientation of the visual pathway.

### **Teaching**

Results of research are directly implemented in medical student and postgraduate teaching. Owing to the extensive contacts with colleagues abroad, many foreign students come to the Department of Ophthalmology for at least a part of their study (graduate or post-graduate) and for further education.

### **Selected publications**

Pasutto F et al. Pseudoexfoliation syndrome-associated genetic variants affect transcription factor binding and alternative splicing of LOXL1. *Nat Commun.* 2017 May 23;8:15466

Tsai TI, Joachimsthaler A, Kremers J. Mesopic and photopic rod and cone photoreceptor driven visual processes in mice with long-wavelength shifted cone pigments. *Invest. Ophthalmol Vis. Sci.* 2017, 58:5177–5187

Schrems WA, Schrems-Hoesl LM, Mardin CY, Laemmer R, Kruse FE, Horn FK. Can Glaucomatous Visual Field Progression be Predicted by Structural and Functional Measures? *J Glaucoma.* 2017 Apr;26(4):373-382

Aher AJ, McKeefry DJ, Parry NRA, Maguire J, Murray JJ, Tsai TI, Huchzermeyer C, Kremers J. Rod- versus cone-driven ERGs at different stimulus sizes in normal subjects and retinitis pigmentosa patients. *Doc Ophthalmol.* 2018, 136: 27-43

Augustin VA, Weller JM, Kruse FE, Tourtas T. Fungal Interface Keratitis After Descemet Membrane Endothelial Keratoplasty. *Cornea.* 2018 Nov;37(11):1366-1369

Menzel-Severing J, Zenkel M, Poliseti N, Sock E, Wegner M, Kruse FE, Schlötzer-Schrehardt U. Transcription factor profiling identifies Sox9 as regulator of proliferation and differentiation in corneal epithelial stem/progenitor cells. *Sci Rep.* 2018; 8(1): 10268

### **International cooperations**

Prof. Dr. M. Greiner, Department of Ophthalmology and Visual Sciences, University of Iowa Carver College of Medicine, Iowa: USA

Prof. Dr. S. Kinoshita, Department of Frontier Medical Science and Technology for Ophthalmology, Kyoto Prefectural University of Medicine, Kyoto: Japan

Prof. Dr. N. Koizumi, Department of Biomedical Engineering, Faculty of Life and Medical Sciences, Doshisha University, Kyotanabe: Japan

Prof. T. Aung, Singapore Eye Research Institute, Singapore National Eye Centre: Singapore